In Vitro Differentiation of T cells from Human Embryonic Stem Cells.

Grant Award Details

In Vitro Differentiation of T cells from Human Embryonic Stem Cells.

Grant Type: SEED Grant

Grant Number: RS1-00295

Investigator:

Name:	Ellen Robey
Institution:	University of California, Berkeley
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $477,894

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: In Vitro Differentiation of T cells from Human Embryonic Stem Cells.

Public Abstract:

White blood cells are the main players of human immunity in defense against infection. Defects in CD4 T white blood cells, for example, can lead to the devastating infections observed in AIDS patients and patients with a genetic immunodeficiency syndrome ("bubble boy" syndrome). A normal immune system can recognize and attack pathogens but not "self". This is achieved by rigorous selection and "education" during development of T or B white blood cells and by regulatory T cells that suppress occasional "run-away" white blood cells. Glitches in these processes can also lead to equally devastating problems as seen in many autoimmune diseases like type I diabetes, multiple sclerosis and rheumatoid arthritis. Thus, the availability of T cells or regulatory cells could lead to therapies for many human diseases.

A major limitation in using T cells in therapy is the lack of available primary T cells generated in the laboratory. Attempts thus far to generate T cell precursors in a tissue culture dish from the existing NIH approved embryonic stem (ES) cell lines have had only limited success, perhaps due to the partial white blood cell potential of these particular lines. Efficient conversion of T cell precursors into mature T cells or regulatory T cells in a tissue culture dish have also not yet been achieved.

In this seed grant application, we propose to test a series of new (non-federally approved) human embryonic stem (ES) cells for their abilities to efficiently generate white blood cells precursors and subsequently immature T cells in a tissue culture dish. Conditions to optimize generation of white blood cell precursors and T cell precursors will be sought. We will then examine how to convert mature T cells from T cell precursors by varying the culture conditions to closely mimick the "real" situation in humans. Successful completion of this project would constitute a major first step in the long-term goal of using human T cells (that can attack pathogens, but do not react to one's own organs) in therapy. Examples of possible clinical therapy include administration of regulatory T cells in preventing autoimmune attacks in a variety of aforementioned autoimmune diseases. Availability of T cells specific for proteins found in tumors could be used to treat cancer, and mature T cell populations could be used to restore immune function of AIDS patients and to improve the short-term survival of bone marrow transplant recipients.

Statement of Benefit to California:

Successful completion of this seed project, with the eventual goal of a comprehensive research project in T cell differentiation from human ES cells, will have a major impact in devising a new immune therapy to combat a variety of diseases. California has many cancer and AIDS patients and many of its citizens are suffering from debilitating autoimmune diseases. The availability of normal and regulatory T cells generated in the laboratory and tailored to individual person will pave a way to a novel T cell therapy to treat Californians suffering from many currently incurable diseases. At the same time, we will also significantly increase our basic understanding of how the human immune system develops, which might eventual lead to novel invention of diagnostic or therapeutic tools. Furthermore, the project could serve as a basis for biotech companies in California to exploit the therapeutic goals of this research endeavor.

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